

Application/Control Number: 10/574,526  
Art Unit: 1616

IN THE SPECIFICATION:

*The nature of the invention:*

This invention is delineating an aqueous solution containing the unique molecule  $O^4$ . Though previously described as being "transient in nature" it has been found that the solution containing this  $O^4$  has unique chemical and biologic properties that will enable it to be used as a therapeutic modality. The aqueous solution containing  $O^4$  has been determined to have a shelf life of up to 3 years.

The  $O^4$  has been identified in several settings using Mass Spectrometry.

Independent research in July 2003 was conducted by molecular scientist Allan Xu, Ph.D. of SFBC International 401A Industrial Drive, North Wales, PA 19454. Using Mass Spectrometry to analyze this oxygen containing solution Dr. Xu concluded that there was a unique molecule of molecular weight 64 (the weight of 4 oxygen molecules). in the oxygen containing solution.

The presence of  $O^4$  in this aqueous solution was confirmed by use of High Resolution Mass Spectrometry. The Perkins Elmer Elan® 6000 ICP Mass Spectrometer confirmed the presence of greater than 23% of  $O^4$  in the oxygen containing aqueous solution.

Additional tests to document the presence of oxygen in the solution included the LaMotte EDO/AG30 DO Test Kit. Results of this test indicated 920 p.p.m. (mg/L) of oxygen in the solution. Prior to the measurements the solution was diluted 100:1. Therefore the actual mathematical extrapolation would be 92,000 (920 x 100=92,000) p.p.m. (mg/L).

It is agreed that oxygen species can be transient in nature particularly when they reach the tissue level. However, the life of the oxygen contained in this unique solution has been determined as being 3 years duration. What this demonstrates is that the oxygen remains in the aqueous solution for 3 years.

*The state of prior art and the predictability or lack thereof in the art:*

Since many disease conditions result in tissue hypoxia there is tremendous value in being able to provide oxygen locally to treat these conditions. One method to assess the amount of tissue oxygen is by using Transcutaneous Oximetry. Transcutaneous Oximetry is a non-invasive method of measuring the partial pressure of Oxygen in tissue.

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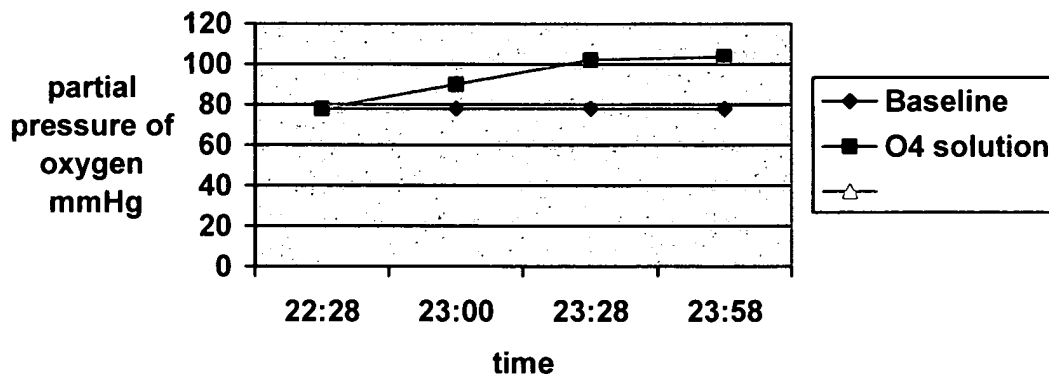
Transcutaneous measurement of partial pressure of oxygen and partial pressure of carbon dioxide has been performed since 1974. It was first used to monitor respiratory balance in premature infants. Data obtained from hemogas analysis correlated with the transcutaneous tissue data ( $r=.98$ ). Applications for use of the transcutaneous tissue measurement are based on this correlation and blood oxygen transport.

The Transcutaneous Tissue Oxygen Monitor manufactured by Radiometer America, Inc. (810 Sharon Drive, Westlake, Ohio 44145) may be used to diagnose conditions and to interpret transcutaneous oxygen conditions. The Transcutaneous Tissue Monitor has been validated and substantiated for use in treatment of conditions in which oxygen levels are important.

The United States Federal Government has accepted this device as useful for patient diagnosis and treatment in conditions where oxygen levels are being assessed. Established codes for billing are CPT code 93922 and CPT 93923. Services that are billed using this diagnostic technique include diagnosis of tissue conditions and Physician reimbursement for interpretation of results.

Using the Transcutaneous Oxygen Monitor the partial pressure of oxygen in tissue was measured in skin without treatment to establish baseline. After baseline levels were assessed a solution containing  $O^4$  containing formulation was applied topically to the skin. The baseline levels of partial pressure tissue oxygen were compared with partial pressure levels after the  $O^4$  containing solution was applied.

#### Effects of $O^4$ on transcutaneous measurements



#### Results & Conclusions

The Radiometer America Transcutaneous Tissue Monitor was used to assess the partial pressure of oxygen in tissue at Baseline and after application of a solution containing  $O^4$ . Measurements of the skin at baseline (skin which did not have the  $O^4$  containing solution applied) had a mean of 78mmHg. After application of the  $O^4$  containing solution there was a gradual incline of the measure levels of partial pressure of oxygen in tissue. The  $O^4$  containing solution increased the baseline tissue oxygen levels to a mean of 102 mmHg. This level was reached gradually and was maintained for at least 90 minutes

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after application. This represents an increase of 28-30% in tissue oxygenation. The trend of these results was demonstrated consistently across studies.

Medical literature widely supports the use of supplemental oxygen to facilitate healing of various disease conditions. The use of the Transcutaneous Monitor to assess peripheral arterial disease has been demonstrated (G.Andreozzi). Hypoxia (lack of oxygen) in wounds has been demonstrated to result in a high risk of non-healing. Additionally, the importance of oxygen has been indicated in many other disease conditions including ophthalmic, cardiovascular and inflammatory disease conditions to name a few. Hypoxic injury to these tissues as a result of no oxygen can exacerbate many disease conditions.

The ability to increase the local oxygen level in tissues, especially in tissues further compromised by hypoxia represents a significant advance in medical science. Successful treatment of many medical conditions with hyperbaric oxygen supplementation demonstrates the importance of oxygen treatment. The Federal Government authorizes billing for use and treatment of conditions with hyperbaric oxygen. We have demonstrated that with the use of the  $O_4$  containing solution a localized hyperbaric condition can be created. This localized hyperbaric condition can result in successful treatment of many conditions.

The long shelf life of 3 years demonstrates that the tetrameric oxygen exists more than transiently. Further, it has been demonstrated that by applying a solution containing the tetrameric oxygen existing tissue oxygen levels can be significantly increased and an extended duration of tissue penetration occurs. Using a transcutaneous monitor this increase has been demonstrated for more than 90 minutes. The nature of the invention has been demonstrated in that by increasing tissue oxygen levels a localized hyperbaric condition is created and a therapeutic effect can be reached.

*The amount of direction or guidance present and the presence or absence of working examples:*

Research (above) has been provided of the use of tetrameric oxygen in a solution applied topically to skin. In these studies the tissue oxygen was increased in skin as a result of the application of tetrameric oxygen containing solution. Although skin was used as a representative example of the ability of this oxygen to increase tissue oxygen it can be assumed that the application of this solution to any tissue would result in localized increases in the partial pressure of oxygen in that particular tissue.

*The breadth of the claims and the quantity of experimentation needed:*

Several objective methods (see above) of testing have demonstrated the existence of the unique species tetrameric oxygen ( $O_4$ ) contained in the aqueous solution. The fact that this molecule is contained within an aqueous solution allows the mixture of it into any other delivery system wherein an aqueous component may be included. For example

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to make up a gel or semi-solid the tetrameric oxygen may be included as the aqueous component. This would then allow the tetrameric oxygen to be delivered in alternative formulations and consistencies.

The validation of oxygen as a construct for therapeutic treatment is widely demonstrated in the literature. Hence this invention is merely expanding the options available for successful delivery of oxygen to various tissues and disease conditions. Since the solution is aqueous the composition, delivery systems and method of delivery can be altered to include a wide array of options. It is an awesome medical breakthrough that can help many patients with many different conditions. The shelf life and prolonged tissue absorption when applied directly to tissue demonstrate that this solution is stable enough to be used in medical treatment. The fact that it is contained within an aqueous formulation widely increases options for medical professionals and patients.

### REMARKS

The above response to the office action is an attempt to address the issues raised in the Office Action dated April 8, 2008. Any issue which has not been addressed is inadvertent.

I certify that this response to office action was deposited in the United States Express Mail as of October 8, 2008.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Judith Boston', with a large circular flourish on the left and a stylized 'D' on the right.

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